Medical School Hotline

The Role of Genetics in (Continuing) Medical Education in Hawaii

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Medical education has to be a lifelong professional commitment for physicians. There has been a rapid evolution of new techniques, new concepts, and, unfortunately, new jargon in the field of Genetics. To understand the role of heredity in human disease, it is imperative that past as well as present students acquire, and continue to add to, this new lexicon.

Gene regulation is no longer a simple concept of "one gene, one protein." Getting from the trinucleotide code in the DNA to protein function in cells is a tortuous path marked by many yet-to-be-understood road signs. *Promoters* initiate gene transcription, *introns* are "spliced out," and *exons* code mRNA. mRNA is further processed and finally allowed access to tRNA to translate its code into amino acids that form proteins like beads on a string. These proteins are still usually only functional after further modification. Concepts such as "alternative mRNA splicing" or "post translational" modification-producing proteins with different structure and function in different tissues have altered dramatically our understanding of organ specificity and selectivity in genetic disorders.

One explicit goal of Genetics is to better understand and treat human diseases. Defining the cause of gene differences producing altered function has confirmed some traditional concepts but has also provided many surprises. In several enzyme disorders, the confusing interfamilial clinical *variability* has been shown to be due to different defects of the gene with profoundly different effects on protein stability and function. Understanding *intrafamilial* variability has proven more difficult and we are often left with invoking such unsatisfactory concepts as gene-gene or gene-environment interaction. Furthermore, finding different abnormal genes that cause similar phenotypes has confirmed one theory of *genetic heterogeneity*, yet not fully explained is the corollary, ie, defects in the same gene can give totally different phenotypes!

Naively, early workers thought that once we discovered the gene for a certain disorder we would have a consistent way to test for the presence or absence of the defect. Soon it became apparent that some disorders are caused by many different mutations and simple screening for those disorders would not be practical. Fortunately, knowing specific mutations in a family provides for more accurate diagnosis, both symptomatic and pre-symptomatic, and to help in prenatal testing.

Delineating these new genetic concepts has helped us to understand disturbed organogenesis better, inherited resistance to disease, inherited susceptibility to cancer, and is beginning to provide new diagnostic tests and novel therapeutic agents. Genetic testing is now routinely applied in the laboratory. For example, detection of microbial genetic material in tissue samples helps to confirm their role in pathogenesis. Genetic markers are routinely looked for in tumors to understand disturbed cellular regulation. Oncogenes and tumor suppressor genes have been found throughout the genome and predicting susceptibility to certain tumors will hopefully allow individuals better access to preventive measures in the future. DNA typing has become standard for paternity disputes and forensics in some states.

Primary care physicians, particularly in the climate of managed health care, will have to convey basic genetic information to their patients while still being faced with the challenge of knowing when to refer individuals or families for more comprehensive evaluation with genetic specialist. Treatments have already been impacted. Specific metabolic "co-factors," recombinant DNA-produced hormones and enzymes, and even "corrected gene" therapy are now available for rare genetic diseases. Educational and supportive genetic counseling is becoming increasingly more demanding and allied health care profession-

als are playing a larger role, requiring physicians to become educated about other disciplines and the advantages of using these colleagues. Obstetric specialists must be able to identify pregnancies at high risk for fetal abnormalities, and are required to understand and perform increasingly complex fetal diagnostic tests. And finally, to understand state- of-the-art chromosomal and molecular DNA tests, all physicians will need current information updates from our laboratory colleagues.

The rich ethnic diversity in Hawaii means different genetic disease susceptibilities have been introduced along with diverse cultural heritages. Also, each population has its own range of normality for routine and special tests, which have to be considered in medical evaluations and treatments. Ongoing research at the University of Hawaii, the Cancer Research Institute, and other community-based, federally funded programs is providing valuable information about genetic variability as related to various diseases in our population unique to the nation and the world.

In the face of this flood of new information, all Hawaii health professionals need to maintain an up-to-date understanding of relevant genetic advances. The UH faculty is actively teaching students at every level of training, as well as medical practitioners and health professionals throughout the state. In addition lay education impacts in both directions. Well-informed physicians educate their patients and families and direct them to other resources. The well-informed consumers, through networks such as support groups, learn about their specific health-related problems and update their providers on current information. In addition, family education is an integral part of every genetic counseling session. Health care professionals, including clinical geneticists and research geneticists, provide education in cooperation with all branches of the mass media.

Finally, clinical care is driven by ongoing research, both basic and clinical (applied). Genetic research tools are being used in research to add to knowledge that can benefit people everywhere. Basic genetic research in Hawaii has ranged from studying evolutionary, quantitative, and cyto-genetics, gene-environment interactions, embryo-genesis, and cell-cell communications in fungi, insects, birds and mammals. In clinical research, an example of the marriage of the research expertise in the state with the unusually diverse ethnic population has produced clinically useful information about inherited thalassemia. Data from the largest known family with inherited precancerous von Hippel Lindau disease were instrumental in locating and identifying the gene that is mutated; special DNA tests are now being used to identify gene carriers in this family. Collaborations with colleagues elsewhere include trying new treatment for otherwise lethal a-thalassemia, assessing the relation of muscular dystrophy with eye abnormalities, and looking for a human obesity gene.

The 21st century physician will likely be in an unprecedented position compared to the 2,000-year-old model. The human *genome* will be nearly characterized. It is hoped the information learned will confirm other traditional concepts but will just as likely provide even more startling discoveries. This newly gained ability to understand the role of heredity in causing and preventing disease will provide for even more innovative *manipulations*. It is hoped that researchers and physicians will approach this opportunity in awe of the power of the tools and continue to show respect for the uniqueness of their species. Lay education will have to parallel medical education so public fears of misuse will not outweigh the benefits. And finally, society will have to develop a multidisciplinary forum to monitor these approaches to safeguard the public.

Military Medicine

Tripler's Travels: Reports from the Field

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The medical staff at Tripler Army Medical Center (TAMC) are routinely called to provide health care away from home. There are a number of different types of missions supported by physicians and ancillary staff from TAMC. These include military deployment, humanitarian relief missions, medical assistance to civilian populations, disaster relief services, and support of United Nations' peacekeeping missions.

Training for these types of missions is integral to the military physician's job. A series of training courses in field medical operations is routinely taken by all Army physicians. A combat casualty care course (C-4) is mandatory for Army interns. This experience provides training and certification in advanced trauma life support (ATLS) and an intensive exposure to operational field medicine. The course is taught at Fort Sam Houston, San Antonio, Texas, and is usually a welcomed interlude during the rigors of internship.

Advanced training in specialized areas is available for physicians with particular interests, or for those who will require skills for a specific mission. The Army conducts so-called short courses of 1-week to 4-week duration in subjects such as medical management of chemical, biological and nuclear injuries, field sanitation, arctic survival skills, environmental medicine, tropical medicine, hyperbaric medicine, aviation medicine, and preventive medicine. Residency programs